

Claims

1. Receptor binding conjugate,
characterized in that it consists of three components; (1) an antibody or antibodies preferably of IgG or IgM class, or fragments or constructs (e.g. minibody) thereof, (2) a radionuclide or a mixture of radionuclides and (3) folate or a folate derivative, wherein or not the conjugate possesses a dual target binding ability.
2. Receptor binding conjugate according to claim 1,
characterized in that the antibody or antibodies are polyclonal IgG without dual binding ability.
3. Receptor binding conjugate according to claim 1,
characterized in that the radionuclide can be selected from the group consisting of alpha emitters, beta emitters, gamma emitters, position emitters and/or x-ray,
4. Receptor binding conjugate according to claim 1,
characterized in that the radionuclide is an alpha emitter, such as ^{211}At , ^{212}Bi , ^{213}Bi , ^{212}Pb , ^{225}Ac , ^{223}Ra , ^{224}Ra or ^{227}Th .
5. Receptor binding conjugate according to claim 1,
characterized in that the radionuclide is an beta emitter, such as ^{131}I , ^{90}Y or ^{153}Sm .
6. Receptor binding conjugate according to claim 1,
characterized in that the radionuclide is ^{211}At or ^{125}I .
7. Method to prepare a receptor binding conjugate,
characterized in that it consists of three components; (1) an antibody or antibodies preferably of IgG or IgM class, or fragments or constructs (e.g. minibody) thereof, (2) a radionuclide or a mixture of radionuclides and (3) folate, wherein the method uses standard procedures for radionuclide labelling and folate labelling of the antibody.

8. Method to prepare a receptor binding conjugate, characterized in that it comprises preparing a conjugate consisting of 1-50 folate units attached to an antibody, fragment or construct, labelled with any radionuclide useful for radiotherapy, with or without using a linker between the radionuclide and the antibody, fragment or construct, and performed so that the radiolabelling may be carried out before, simultaneous, or after the folate labelling of the antibody, fragment or construct.
9. Method according to claim 8, characterized in that the radionuclide can be selected from the group consisting of alpha emitters, beta emitters, gamma emitters, positron emitters, and/or x-ray.
10. Method according to claim 8, characterized in that the radionuclide is an alpha emitter such as ^{211}At , ^{212}Bi , ^{213}Bi , ^{212}Pb , ^{225}Ac , ^{223}Ra , ^{224}Ra or ^{227}Th .
11. Method according to claim 8, characterized in that the radionuclide is an beta emitter such as ^{131}I , ^{90}Y , or ^{153}Sm .
12. Method according to claim 8, characterized in that the radionuclide is an emitter useful for radioguided surgery, e.g. ^{125}I .
13. Method according to claim 8, characterized in that the antibody or antibody fragment is a polyclonal human antibody, or polyclonal antibody from other species.
14. Method according to claim 8, characterized in that the antibody or antibody fragment is a murine or chimeric or fully humanized monoclonal antibody with or without binding affinity towards an antigen other than the folate binding protein.

15. Method according to claim 8,
characterized in that the antibody or antibody fragment itself has binding affinity towards an antigen other than the folate binding protein, i.e., the conjugate may thereby have dual-receptor affinity when folate is conjugated to it.
16. Use of a folate-antibody-radionuclide conjugate according to claim 1,
to prepare a pharmaceutical solution suitable for injection or infusion into mammals including humans.
17. Use of a folate-antibody-radionuclide conjugate according to claim 16,
to prepare a pharmaceutical solution suitable for injection or infusion into mammals including humans by intravenous, and/or regional, and/or intratumoural route of administration.
18. Method to use a conjugate described in claim 1, to target cells expressing the folate binding protein by means of injection or infusion into mammals including human subjects for the purpose of imaging the receptor containing cells (tissues).
19. Method to use a conjugate described in claim 1, to target cells expressing the folate binding protein by means of injection into human subjects for the purpose of delivering potentially therapeutic radiation to malignant cells (tissues) expressing folate binding receptor(s).
20. Method to use a conjugate described in claim 1, to target cells expressing the folate binding protein by means of injection into human subjects for the purpose of delivering potentially therapeutic radiation to malignant cells (tissues) expressing receptor(s) for folate when the malignant tissue is brain-, lung-, cervix-, ovary- or breast cancer.

21. Use according to claim 16 in combination with folate- and radiolabelled IgG, IgM or fragments thereof and several radioimmunoconjugates and/or other forms of radio pharmaceutical therapy, chemotherapy, external beam therapy, or surgery to treat malignancies expressing folate binding protein.
22. Kit for the preparation of the folate labelled antibody or antibody fragment according to claim 1, comprising a vial containing a folic acid solution and a vial containing a coupling activating agent (e.g. 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) in solution, which can be used by combining the two vials content prior to adding it to a solution containing the antibody or antibody fragment.
23. Kit according to claim 22, for the preparation of folate and radioisotope labelled antibody or antibody fragments comprising two vials and with a third vial containing a solution with the radioisotope or a ligand, that is either prelabelled or can be labelled subsequently with the radioisotope that can be attached by means of covalent binding or chelation to the antibody or antibody fragment.
24. Preparation of pharmaceutical solutions suitable for radiotherapy or radiodetection based on the dual-binding-ability principle where the active component is a conjugate consisting of (1) IgM, IgG or fragments and constructs (e.g., estrogen or derivative or testosterone or an derivative) with receptor affinity other than that of the antibody itself.